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Chapter

Microbiome - The Power House of Health and Disease

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Abstract

The field of microbiome is an exciting and rapidly expanding research over the past few decades that have become a topic of great scientific and public interest. Microbiome comprises a complex collection of microorganisms, with their genes and metabolites colonizing different body niches in a deep symbiotic relationship in the aspect of both health and diseases. Microbial populations vary across the body sites, driven by different environmental condition, immunological factors and interactions between microbial species. It is now well known that the microbiome interact with their host, assisting in the bioconversion of nutrients and detoxification, boosting immunity and protecting against pathogenic microbes, maintaining individuals' health. A wide range of environmental factors can have an impact on gut microbiota imbalance, which has a strong link to health and disease. The microbial role in basic biological processes as well as the development and progression of major human diseases like infectious diseases, liver diseases, gastrointestinal cancers, metabolic diseases, respiratory diseases, mental or psychiatric diseases, and autoimmune diseases. Therefore, a perfect and sensitive balanced interaction of microbes with the host is required for a healthy body. With recent advances in genome sequencing and 'meta-omics' tools, culture-independent analyses of microbiomes have been made possible, thus accelerating the progress of microbiome research by leaps and bounds.

Keywords: data analysis, dysbiosis, microbiome, metagenomics, microbiota, probiotic

1. Introduction

Microbes inhabit almost all human body parts and play a critical role in human health and disease. Research has increasingly focused on the diverse microbial communities that interact with the host to influence disease processes as modern microbiology and next-generation sequencing technologies have evolved. The term 'microbiome' refers to the complex blend of microorganisms such as bacteria, bacteriophage, viruses, fungi, single-celled animals and their genes as well as metabolites. Colonizing different body niches which contribute in big ways to human health and wellness. As microbial communities, also known as the microbiota, microorganisms, or microbes, coexist and interact with one another and with the surrounding environment. The microbial communities within our body are highly personalized and considered as unique to each individual as

their fingerprints [1] also unique to each body sites [2]. This can also be referred to as the metagenome of the microbiota. The word “microbiome” was coined by Joshua Lederberg, who was the first to use it to “symbolize the ecological community of commensal, symbiotic, and pathogenic microorganisms that literally occupy human body space and have been largely overlooked as health and disease determinants” [3]. Over time, the term microbiome has evolved not only to refer microbiota, but also to the genetic information and the genomes of the microorganisms themselves. It is now well known that the microbiome interacts with its host and also involved in basic human biological processes, modulating the metabolic phenotype in the bioconversion of nutrients and detoxification, influencing innate immunity and protecting against microbial infections. Microbiota boosts the immune system, breaks down potentially hazardous dietary molecules, and synthesizes vitamins like vitamin B12, thiamine, riboflavin, and vitamin K, which is required for blood coagulation [4]. Microbiome is home to trillions of symbiotic microorganisms in which some of these are useful, and some are harmful and it supports many physiological functions, helps in maintaining the integrity of our gut lining, and protects us from disease and infection. Therefore, a perfect and sensitive balanced interaction of microbes with the host is required for a healthy body. The microbiota has many more metabolic genes than the human genome and provides unique enzymes and biochemical pathways to humans [5]. Furthermore, many of the positive metabolic macrobiotic activities for the host are engaged in either food acquisition or xenobiotic processing, such as the metabolism of undigested carbohydrates and vitamin production [6].

Second, through competitive exclusion and the generation of antimicrobial compounds, the human microbiota acts as a physical barrier, protecting its host from invading pathogens [7].

Understanding how microbial metabolites influence the health or disease status would have a significant impact on treating diet related diseases [8]. Microbes that cause disease build up over time, affecting gene activity and metabolic processes and causing an incorrect immune response to substances and tissues that are normally present in the body. Autoimmune diseases tend to be passed down through generations via microbiome inheritance rather than DNA transmission [9]. Recent studies revealed that the associated microbes stimulates the normal development of the humoral and cellular mucosal immune systems and the signals and metabolites of microorganisms can be sensed by the hematopoietic and non-hematopoietic cells of the innate immune system and translated into physiological responses [10]. Often, reduction in microbial diversity and outgrowth of specific species can induce negative effects like inflammation or infection [11]. However, most of the microbial taxa and species of the human microbiome are still unknown. Without revealing the identity of these microbes as a first step, we cannot appreciate their role in human health and diseases [12].

There are plenty of projects trying to decode the human genome by sequencing all human genes. In a similar way, the microbiome has been subject to intensive efforts to unravel all its genetic information. Advances in omics-based techniques have contributed to a better knowledge of the microbiome and the many factors that influence its microbial composition. Understanding the entire spectrum of the “microbiome’s” role in health and disease is still in its infancy. Our bacterial flora clearly plays a far larger influence in systemic disorders than previously thought [13]. High throughput sequencing reveals the amazing complexity and extent of the microbial communities that reside within or upon us therefore various computational approaches are available to analyze the microbiota on an unprecedented scale [14]. Recent scientific advances in genetics mean that humans know a lot more about the microbes in the body. Researchers from across the globe are investigating how changes in the

microbiome are linked to, or perhaps cause, illnesses, as well as developing new therapeutic ways to modify the microbiome to cure disease and restore and support health. In addition, microbiome research is gaining tremendous interest as documented by the explosion in publications with more than 20,000 articles published in 2020 alone. The rapid development of new molecular tools such as transcriptomics, metagenomics, and metabolomics has aided in the recent advancement of microbiome results linked to humans. These fast evolving recent technologies are enhancing our ability to comprehend the human body and the microbiome that affects health. Researchers need to conclude with future directions and how to convert the basic science into translational medicine and development of innovative microbiome-based therapy.

2. Microbiome's evolution

Microbiome are the home tract of wide range of microorganisms that can be commensal, symbiotic, or toxic to all multicellular organisms, including plants. The microbiota includes bacteria, archaea, protists, fungi, and viruses, all of which have been shown to be vital for their host's immunologic, hormonal, and metabolic balance [15]. Microbial communities live in multiple body sites in humans and animals (including the stomach, oral cavity, esophagus, skin, and vagina) and interact with and influence their hosts' immune system and metabolism. In addition, microbes have developed alongside humans and are now an essential component of life, performing a variety of essential roles. Due to changes in environmental parameters such as temperature, pH, oxygen, and nutrition availability, their composition varies greatly between body locales and specific biogeography. Although much has been done to explore its diversity, a full understanding of our microbiomes demands an evolutionary perspective. At the strain level, microbial evolution may occur (e.g., when advantageous mutations in specific genes drive adaptation to new selection pressures) selection may also enhance the frequency of a specific microbial taxon, causing the adaptive microbiome's microbial taxa to be lost [16]. The microbiome can evolve at two levels: first, each individual microbe is subjected to evolutionary processes (mutation, selection, migration, drift, speciation, etc.), and second, a host species' microbiome can evolve by incorporation and elimination of microbial taxa, or by changes in their relative abundances as a consequence of these evolutionary processes [17].

Interestingly, mammals that have independently evolved on herbivorous diet often exhibit similar microbiomes [18]; however, this is not the case of panda bears, whose microbiome resembles that of their carnivorous and omnivorous close relatives, despite the panda's herbivorous diet, probably due to phylogenetic constraints [19]. The compositional overlap between the gut microbiota of species populations in the western hemisphere correlates with their geographic proximity in most mammals, and each geographic location has a distinct microbiome composition that is not attributable to the diets or evolutionary histories of the mammals living there, suggesting that horizontal transmission also shapes the microbiome [20]. Because one species and its associated microbiome serve as the meal for the paired predator, this link is most visible in sympatric predator-prey groups. The structure of the relationships in primate species is unknown, but they are likely to follow some of the same patterns.

It is important to remember that the microbiome is a complex and dynamic ecosystem and multiple overlapping factors shape the microbiome composition and it is unique in each individual, and the differences among individuals are largely compared to the typical biochemical differences within a person over time. The gut microbiota is shaped by a variety of factors, including genotype,

dietary composition and mode of delivery, recreational drugs, antibiotic therapy, pre and probiotic treatment, lifestyle (e.g., smoking and physical activity), social interactions, and environmental exposure to various xenobiotics. In addition, several other factors are also involved including (i) Diet. The types of food that a person consumes can have a significant impact on gut microbiota. (ii) Exposure to pathogens, (iii) Age, (iv) Psychological Stress/Anxiety, (v) Medication/Drug Use, (vi) Tobacco Use, and Alcohol Consumption (vii) Physical Activity [21]. One important factor emerging from the research advances is the importance of microbial diversity. In healthy settings, an individual's microbiota is more diverse than in sickness, when diversity is diminished. Low microbiome diversity has been linked to metabolic inefficiency, skin issues, gastrointestinal problems, and low-level inflammation.

Because of the biological interaction of the organisms with the immune system throughout time, the indigenous organisms in the human body are well adapted to the immune system. A shift in the gut microbial flora plays a crucial impact in human health and disease pathogenesis. These changes are caused by a combination of factors, including lifestyle and the existence of an underlying disease. Dysbiosis makes the host more susceptible to infection, the type of which varies depending on the anatomical place. The precise metabolic activities and functions of these microorganisms within each bodily location are accounted for by the inherent diversity of the human microbiota. As a result, it's critical to comprehend the human microbiome's microbial composition and behaviors as they relate to health and disease. The microbiome can affect many physiological processes in our body, including immune system development, the ability to process dietary polysaccharides, vitamin and hormone production, pH regulation, processing and detoxification of environmental chemicals and maintenance of the skin and mucosal barrier function [22, 23]. There has been a boom of research into how the microbiota of the gastrointestinal system affects human health and disease, and what treatments might be made, particularly in the last decade (**Table 1**).

Phylum	Class	Characteristics	Examples
Firmicutes	Bacilli; Clostridia	Gram-positive bacteria with a variety of morphologies (rod, coccoid, spiral) and physiologies (anaerobic, aerobic); commensal and helpful bacteria.	<i>Lactobacillus</i> ; <i>Ruminococcus</i> ; <i>Clostridium</i> ; <i>Staphylococcus</i> ; <i>Enterococcus</i> ; <i>Faecalibacterium</i>
Bacteroidetes	Bacteroidetes	Gram-negative; made up of three main classes that are widely spread in the environment, such as soil, ocean, and animal intestines.	<i>Bacteroides</i> ; <i>Prevotella</i>
Proteobacteria	Gammaproteobacteria; Betaproteobacteria	Gram-negative; include a wide variety of pathogens	<i>Escherichia</i> ; <i>Pseudomonas</i>
Actinobacteria	Actinobacteria	Gram-positive; diverse morphology; major antibiotic producers in the pharmaceutical industry	<i>Bifidobacterium</i> ; <i>Streptomyces</i> ; <i>Nocardia</i>

Table 1.
In the human body, the most common bacterial phylum [24].

3. Human microbiome project

The major goal of the human microbiome project is to define the number, diversity and functionality of genes found in all bacteria that live in various parts of the human body on a permanent basis and analyze its role in human health and disease. The gut microbiota expresses around 3.3 million bacterial genes, compared to only 20,000 genes in the human genome. Studies show that manipulating non-pathogenic bacterial strains in the host can help the immune system recover from disorders caused by pathogenic bacteria. An ever-growing number of studies have demonstrated that changes in the composition of our microbiomes correlate with numerous disease states, raising the possibility that manipulation of these communities could be used to treat disease. The microbiome of a person can affect their susceptibility to infectious diseases and contribute to gastrointestinal chronic disorders including Crohn's disease and irritable bowel syndrome. A person's response to a pharmacological therapy is determined by a group of microorganisms. The mother's microbiome may have an impact on her children's health.

Researchers researching the human microbiome are discovering previously unknown organisms and genes all around the world. Various combinations of microbial species have been related to certain human health issues in genetic studies that quantify the relative abundance of different species in the human microbiome. A thorough understanding of the diversity of microbes in the human microbiome could lead to new therapeutics, such as producing more "good" bacteria to cure a bacterial infection caused by "bad" bacteria. The HMP is a road plan for understanding and describing the role of the microbiome in health, nutrition, immunology, and disease.

4. Microbiota benefits of the body

The microbiome is essential for human development, immunity and nutrition. Microbiota boost the immune system, break down potentially harmful dietary components, and manufacture vitamins and amino acids such vitamin B and vitamin K [25]. The major enzymes required for the formation of vitamin B12 are exclusively present in bacteria, not plants or mammals [26]. Bacteria living in and on the human body are not always invaders but beneficial colonizers too. Sugars like table sugar and lactose (milk sugar) are quickly absorbed in the upper portion of the small intestine, while more complex carbs like starches and fibers are more difficult to digest and may end up in the large intestine. By creating digestive enzymes, the microbiota aids in the breakdown of these substances. Short chain fatty acids (SCFA) are produced when indigestible fibers are fermented, and they can be utilized by the body as a food source as well as play a role in muscular performance and possibly the prevention of chronic diseases including cancer and bowel disorders. SCFA has been demonstrated to be effective in the treatment of ulcerative colitis, Crohn's disease, and antibiotic-associated diarrhea in clinical trials [25].

Autoimmune diseases like diabetes, rheumatoid arthritis, muscular dystrophy, multiple sclerosis, and fibromyalgia have been linked to microbiota dysfunction. Microbes that cause disease build up over time, altering gene activity and metabolic processes, leading in an aberrant immune response to chemicals and tissues that are usually present in the body. A healthy person's microbiota will also defend them from harmful organisms that enter the body by drinking or eating polluted water or food such as

Prevotella, *Ruminococcus*, *Bacteroides*, and *Firmicutes* are large families of bacteria found in the human stomach. Anaerobic bacteria such as *Peptostreptococcus*, *Bifidobacterium*, *Lactobacillus*, and *Clostridium* can be found in the colon due to the low oxygen environment [27]. These microbes are thought to prevent harmful bacteria from overgrowing by competing for nutrition and attachment sites on the mucus membranes of the gut, which are a significant site of immune activation and antimicrobial protein production [28, 29]. Autoimmune diseases appear to be passed in families not by DNA inheritance but by inheriting the family's microbiome. Recent studies on gut microbiota modulation suggest that probiotics should be used in the treatment of patients with severe COVID-19 infection, according to the National Administration of Traditional Chinese Medicine and China's National Health Commission [30]. Probiotics are used to prevent secondary bacterial infection and maintain intestinal microbiota balance.

5. Microbiome analysis techniques

Microbiome research is a highly transdisciplinary field with a wide range of applications and methods for studying it. There are a number of different technologies available to study the microbiome. Traditional microbiology has historically focused on the study of individual species as isolated units. In the mid-2000s, advances in DNA sequencing technology spawned a new branch of study known as



Figure 1. Microbiome-researching technologies [32].

metagenomics, which allows for a comprehensive exploration of microbial communities without the requirement for culture. Instead of looking at the genome of a single bacterial strain cultivated in a lab, the metagenomics approach looks at a collection of genomes derived from microbial communities collected in natural settings, providing new insight into the complexity of human microbial populations [31] (**Figure 1**).

The identification of about 70% of human microbiota, which was not possible by the existing conventional microbiological methods, has been made possible by the development of the advanced techniques of metagenomics, metatranscriptomics, and metabolomics [33]. Metagenomic is a biotechnological perspective of studying the genome structure of the DNA directly extracted from their natural source [34]. Scientists have utilized these revolutionary approaches to prove the existence of genes from over a thousand different microbial species in our bodies. The metagenomic technique has the potential to uncover novel genes, gene families, and their encoded proteins that could have major implications in biotechnological and medicinal research. It enables us to investigate the makeup of a microbial population [35] (**Figure 2**).

Currently, multiple multinational organizations such as the HMP project and various other independently functioning programs are constantly generating huge amounts of data relating to metagenomic studies, and their microbiome data collection is managed by the Genomes Online Database (**Table 2**).

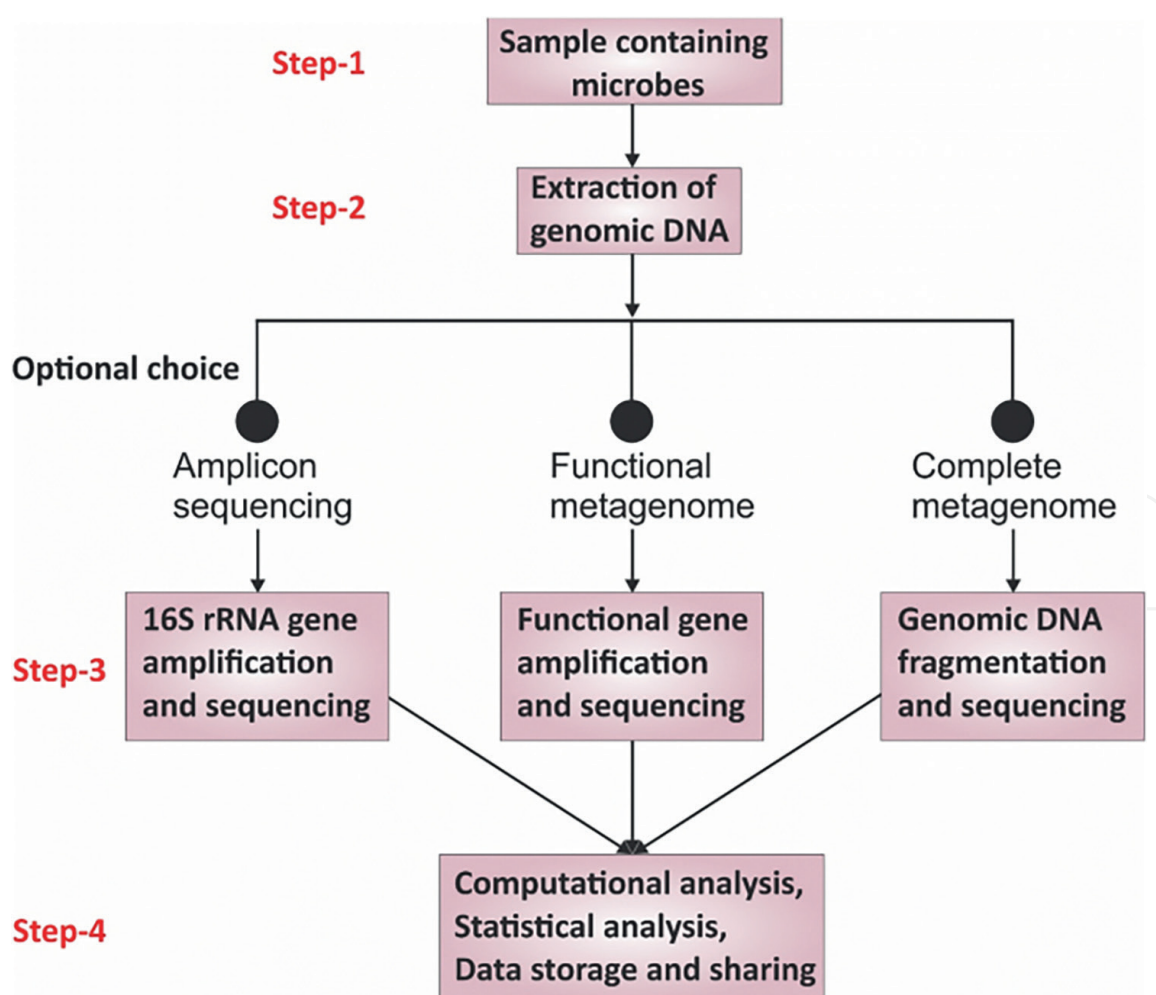


Figure 2. Major steps in the most widely acknowledged genomics strategy for human related microbiome studies are depicted graphically [2].

Methods	Description	Advantages	Limitations	References
Models that are free of germs (GF)	Transplant germ-free in vitro embryos into germ-free moms and rear animals without coming into contact with microorganisms.	To test previously reported relationships, a “blank state” approach was deployed.	Differences in regional makeup are challenging to capture in a compromised, expensive technology that is not reflective of natural microbiome functioning.	[37, 38]
Human sampling	Population is divided into sub groups based on specific characters	Cost effective and relatively easy to access body sample sites	Distinction in regional composition are difficult to capture	[39, 40]
Population scale	Involves sampling from a selected large group of individuals	Large scale conclusion can be drawn, with broadly applicable results	Diversity within individual microbiomes is not considered with purely association based results	[41]
<i>In vitro</i> modeling	Experimental laboratory systems mimicking processes occurring within a living organism	Enables examination of relationship between specific microbes and host	System lacks host level complexity due to reduced microbial communities and simplified environmental structuring	[42]
Patterning of co-occurrence networks	Investigate the impact of organisms and environmental factors on community interactions.	Microbe-microbe interactions and their relationships can be examined to establish ecological network components within microbiomes.	The complexity of the microbial community is reduced, resulting in simpler system operation.	[43]
Direct observation via fluorescence	Probe specific sites or organismal components such as cells, allowing microscopic observation	Taxonomy locality and community organization can be evaluated and screens for specific phenotypes are possible	Photo bleaching can occur	[44]
Bioinformatics	Use of software tools to understand biological data, especially with large complicated data sets	Allows for rapid organization and analysis of data	Often expensive, while drawing association based conclusions	[43, 45]
Association studies	Identify genes correlated with disorders	Can discover correlative relationships between microbes and their hosts	The mechanisms and causative factors underlying correlations remain unknown	[46, 47]

Methods	Description	Advantages	Limitations	References
Meta-omics	Include metagenomics, metatranscriptomics, metaproteomic and metabolomics data collection	Analyze and detect molecular and genetic components and mediators and metabolic profiles	Equipment is highly sensitive and expensive, limiting reproducibility.	[48]
Machine learning models that predict the future	Algorithms are used to find patterns and behavior in datasets.	Use the ease of in situ analysis to find connections between microorganisms and variables.	With association-based and time-consuming data collecting, it's difficult to capture the intricacy of individual microbiomes.	[49]

Table 2.
Methods for analyzing the microbiome [36].

6. A mechanistic link between human health and disease and the microbiome

The microbiome can take up to 40% of our weight and can do many things. The human body is home to a microbiome, which is a networked community of microbes that outweigh the body's own cells. The human microbiome has piqued researchers' interest in recent years due to the microbiome's deep ties to human health. The human microbiome, also known as "our second genome," has developed alongside humans for millions of years and plays an important role in human health. Understanding the human microbiome's composition and function can help us better comprehend its structural and functional features. Understanding the human microbiome and applying metagenomic analysis to specific individuals will considerably improve our understanding of human health and diseases in the future. The study of the human microbiome and metagenome is seen as a new frontier in human genetics.

The majority of study on the human microbiome has focused on the microbes that colonize the human digestive system, as these microbes are thought to have a variety of effects on human health. The digestive system's microbiome is extraordinarily varied, with significant differences in its contents between individuals [50]. Extraneous variables, such as fecal transplantation and dietary intervention, have been proven to modulate the microbiome, which has been shown to be a viable therapeutic method to addressing a variety of health-related disorders [51]. The gastrointestinal tract (GIT) is home to a diverse range of microorganisms, which are connected by microbe-microbe and host-microbe interactions [52]. Microbial guilds (species that share resources) have been discovered to have intriguing traits that can help researchers better understand processes at both the single cell and community levels. Microbes are commensal and mediate digestion, enhance the immune system, and inhibit or prevent infections from penetrating the body under normal physiological conditions. The relationship between the human microbiome and human health is still largely unknown and unexplored, but a decrease in the diversity of the digestive system microbiota has been linked to diseases such as eczema [53], asthma, and inflammatory diseases [54], diabetes and obesity [55], allergies [56], and digestive tract disorders such as IBD (inflammatory bowel disease) [57], and IBS, according to a number of epidemiological studies (irritable

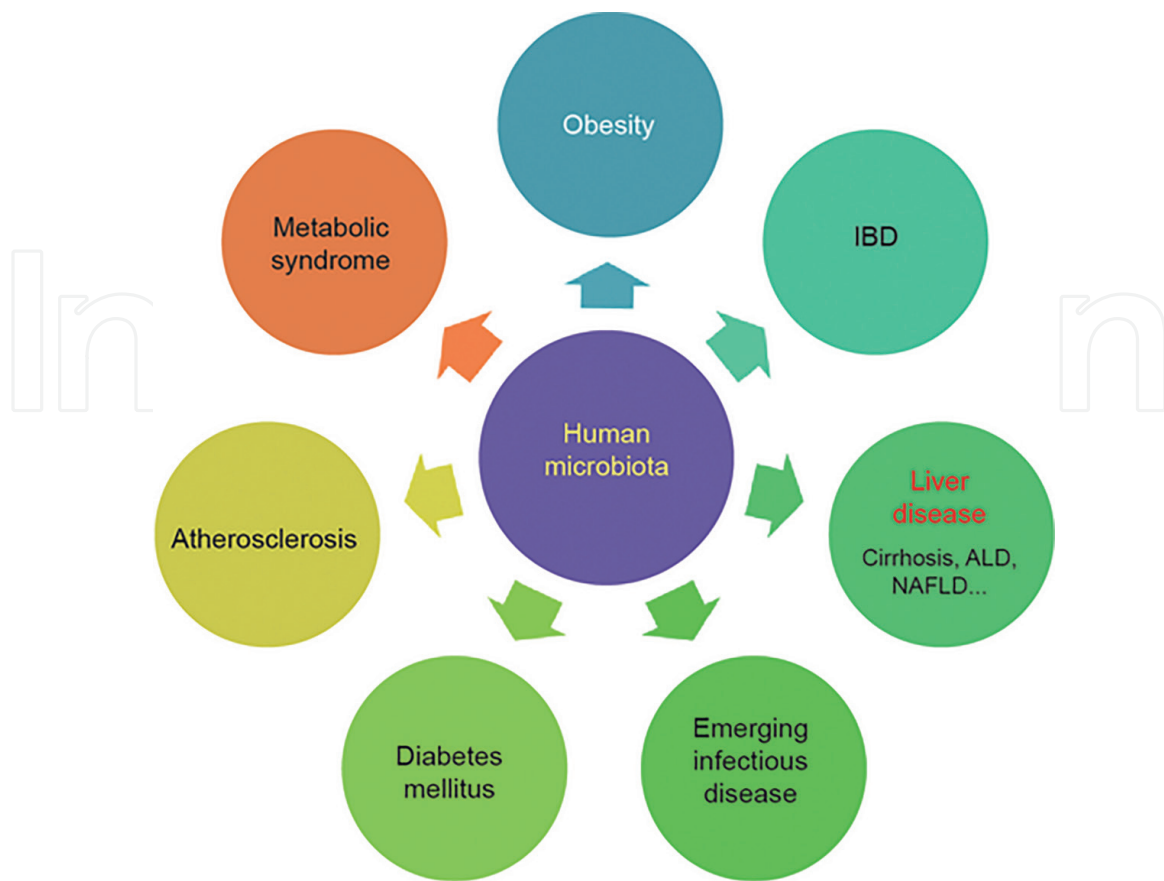


Figure 3. Human microbial symbiosis has a close relationship with diseases of different systems [68].

bowel syndrome) [58]. Chronic fatigue syndrome [59], cancer [60], colitis [61], and bacterial vaginosis [53, 54] have all been linked to dysbiosis (microbial imbalance). A number of recent studies have shown the importance of the gut microbiome in modifying immunological responses, including immune tolerance, via Treg (T regulatory) cell modulation. Short-chain fatty acids (SCFA) have been shown to increase the formation of Treg cells in the gut, according to Geuking et al. [62]. Microbes that live in the gut aid in the breakdown of complex carbohydrates and the usage of polysaccharides [5, 63]. Other health-promoting roles of the gut microbiome include immunological regulation [64], fecal microbiome transplantation [65], metabolism, xenobiotic toxicity, and pharmacokinetics, to name a few [66]. Therefore, patients with respiratory infections and diseases were shown to have gut dysbiosis and concomitant problems, showing gut-lung crosstalk, this phenomenon can also be seen in COVID-19 patients. As a result, boosting gut microbiota using probiotics and other beneficial bacteria is significant in therapeutic applications, and this could be extended to COVID-19 treatment as a new therapeutic approach according to Srinath et al [67] (Figure 3).

7. The function of microbiome in terms of human health

When you realize that there are as many microorganisms in the body as there are human cells, the microbiome's importance seems understandable. The human microbiome is diverse at each body site, such as the gut, skin, mouth, and nasal cavities, where each community of microorganisms is unique. The core microbiome of a person is developed during the first years of life, although it can alter over time as a result of several

factors such as nutrition, drugs, and environmental exposures. Individual vulnerability to various diseases may be determined by differences in the microbiome, which may lead to varying health outcomes from environmental exposures. A healthy microbiome has been found to play a significant role in maintaining good health [69]. Environmental exposures can also alter a person's microbiome, thereby increasing the risk of acquiring diabetes, obesity, cardiovascular and neurological illnesses, allergies, and inflammatory bowel disease. The human microbiome is primarily concentrated in the stomach. These organisms serve a critical role in maintaining and preserving human health. Previous research on the human microbiome project has shown that alterations in the immunological environment can be connected to a dysbiotic gut flora. Dysbiosis has also been related to life-threatening health disorders such as cancer, cardiovascular disease, bowel inflammatory disease, and difficult-to-treat bacterial infections due to antibiotic resistance [70]. A healthy microbiome is a diverse and abundant one, and everything from our nutrition to our surroundings influences how effectively it performs.

However, antibiotic usage and ultra-processed food consumption, for example, are destroying our gut microbiota, making people more susceptible to infections such as *Clostridium difficile* and other diseases. It's only now becoming obvious how important the link between our microbiomes and our health is. The revelation that we can use our microbiome to help us treat or even prevent disease has been perhaps the most significant development. In the last 20 years, the advent of hyper virulent *Clostridium difficile* strains has resulted in a massive increase in infections, with over 20% of cases

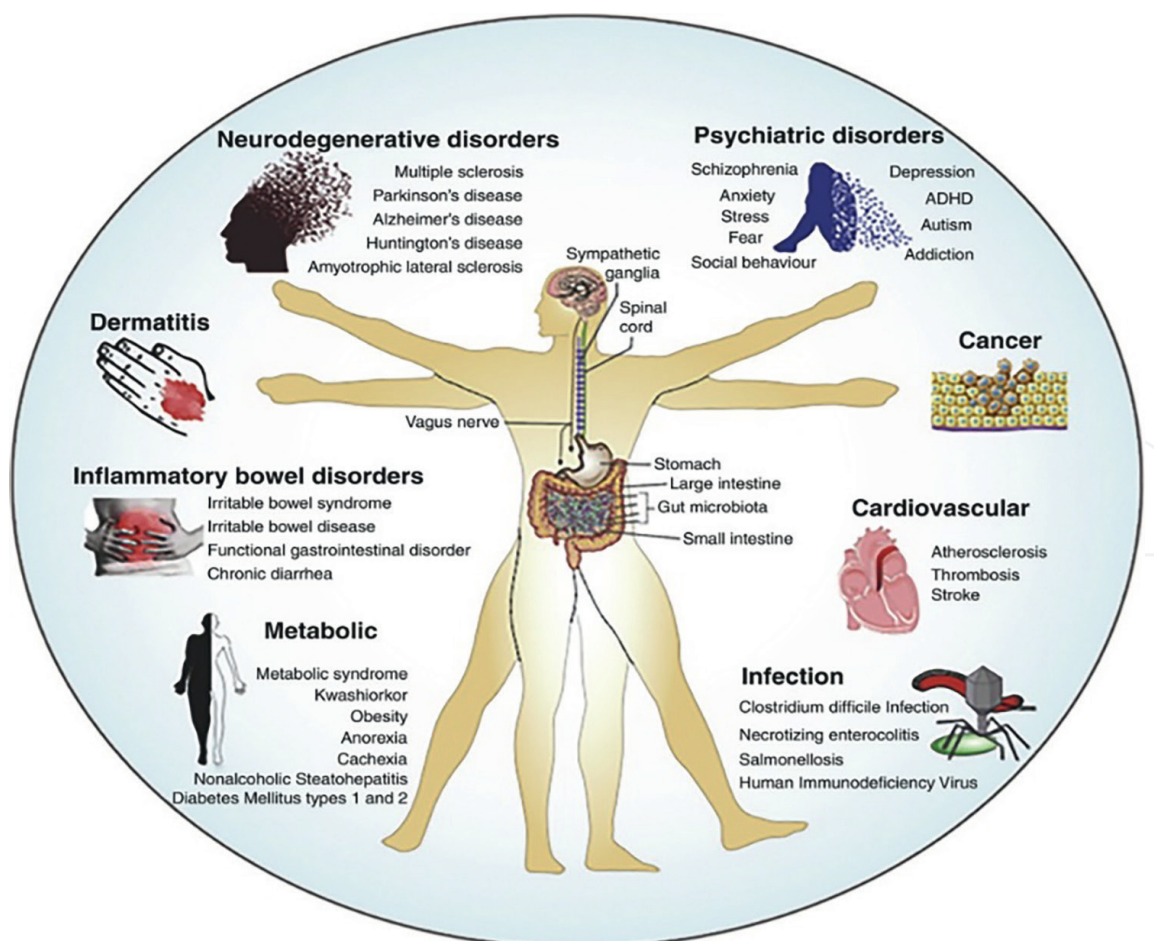


Figure 4. Schematic diagram showing the microbiome implicated in a variety of disorder, including skin, metabolic, and cardiovascular disease, as well as cancer, infection, and neurodegenerative and psychiatric disorders [72].

now involving germs that are drug resistant. The human genome consists of just 23,000 genes, while the microbiome as a whole contains many millions. Scientists are also looking into using microbiota transplants for a wide range of disorders, such as insomnia, Parkinson's disease, HIV, chronic fatigue, multiple sclerosis, obesity, insulin resistance, metabolic syndrome, and autism [71] (**Figure 4**).

8. Antimicrobial resistance

Microorganisms must discover an optimal strategy to coexist with other microbes in a restricted environment in order to thrive. Microbes compete with one another in their surroundings for limited nutrients and space. As a result, they've devised strategies to regulate their own needs by interacting with other microorganisms. Producing antimicrobial compounds that can hinder or kill another germ is one effective technique to do so. Some microorganisms, on the other hand, have evolved mechanisms to survive in the presence of naturally occurring antimicrobials, allowing them to remain a stable member of a microbial community. Antimicrobial resistance can be inherent or acquired in microorganisms. Intrinsic resistance occurs when a bacteria develops resistance to an antibiotic on its own. Microorganisms have had intrinsic resistance mechanisms for millennia, promoting their co-evolution and integration with microbial communities. Antimicrobial medication development and use to treat and eradicate microbial infections is without a doubt the greatest triumph in contemporary medicine. Penicillin, the first mass-produced antibiotic used on a massive scale around the world, saved millions of lives and paved the way for the discovery and development of hundreds of different antimicrobial medications to combat specific infections. Antimicrobial medications have all come from naturally occurring microbial sources, to which certain microorganisms had already evolved innate resistance.

Microbes have developed acquired resistance to antimicrobial medications as a result of increased use of antimicrobial drugs combined with pre-existing resistance. Antimicrobial resistance (AMR) arises when bacteria, viruses, and fungi grow resistant to antibiotics. As a result, infections may become more difficult to remove. AMR is now considered to be one of the most serious risks to world health, food security, and economic development. According to the World Health Organization, at least 700,000 people die each year from drug-resistant diseases, and this number is expected to climb if adequate interventions are not implemented. The overuse and misuse of antimicrobial therapies in a fast rising global economy and population has resulted in a rise in the rate of AMR cases over the last 20 years. Antimicrobials, which are thought to be a panacea for eradicating illnesses, have fueled the emergence of antimicrobial resistance in bacteria.

9. Finding biomarkers in microbiome research

These types of mechanistic tests are currently being carried out in humans by several investigations. The authors assessed the ability of the individual's blood to create cytokines following several antigen challenges in 500 European-ancestral individuals in the Netherlands, and then linked this with data from their gut metagenome. According to the findings, the yeast *Candida albicans* had a particularly strong influence on the host's TNF-alpha response [73]. These investigations are particularly

relevant when dealing with persons who have naturally occurring genetic knockouts or variant alleles. As has been proven for Parkinson's disease, these human genetic variants may enable microbially caused disease that may be investigated in mice with analogous null or variant genetic changes [74].

Characterizing microbial biomarkers offers a lot of promise for precision medicine, and it's a straightforward method to get microbiome research into clinical practice. For example, we know that bacterial probiotics (living bacteria purposely introduced to an animal to have a therapeutic effect) can be utilized to augment immune checkpoint blockade therapy for melanoma patients based on landmark animal studies [75]. Microorganisms in the gut have been identified as biomarkers for diagnosis that can predict if patients are at risk of developing checkpoint blockade therapy after studying the microbiomes of melanoma patients prior to immune checkpoint blockade medication.-colitis caused by a blockage [76].

These prospective studies are critical for correlating the structure, function, and metabolic products of microbial communities to health consequences. Many ongoing investigations, such as the National Institutes of Health Common Core program. Environmental Influences on Child Health Outcomes (ECHO: <https://www.nih.gov/echo>), now provide the infrastructure to sequence healthy, susceptible, and diseased participants to examine how lifestyle and environmental experiences shape the development of immune, endocrine, and neurological conditions. Although single time point investigations of birth cohorts show fascinating statistical relationships [77], longitudinal prospective studies accompanied by mechanistic tests in animal models are needed to determine if a specific microbiome causes disease (**Figure 5**).

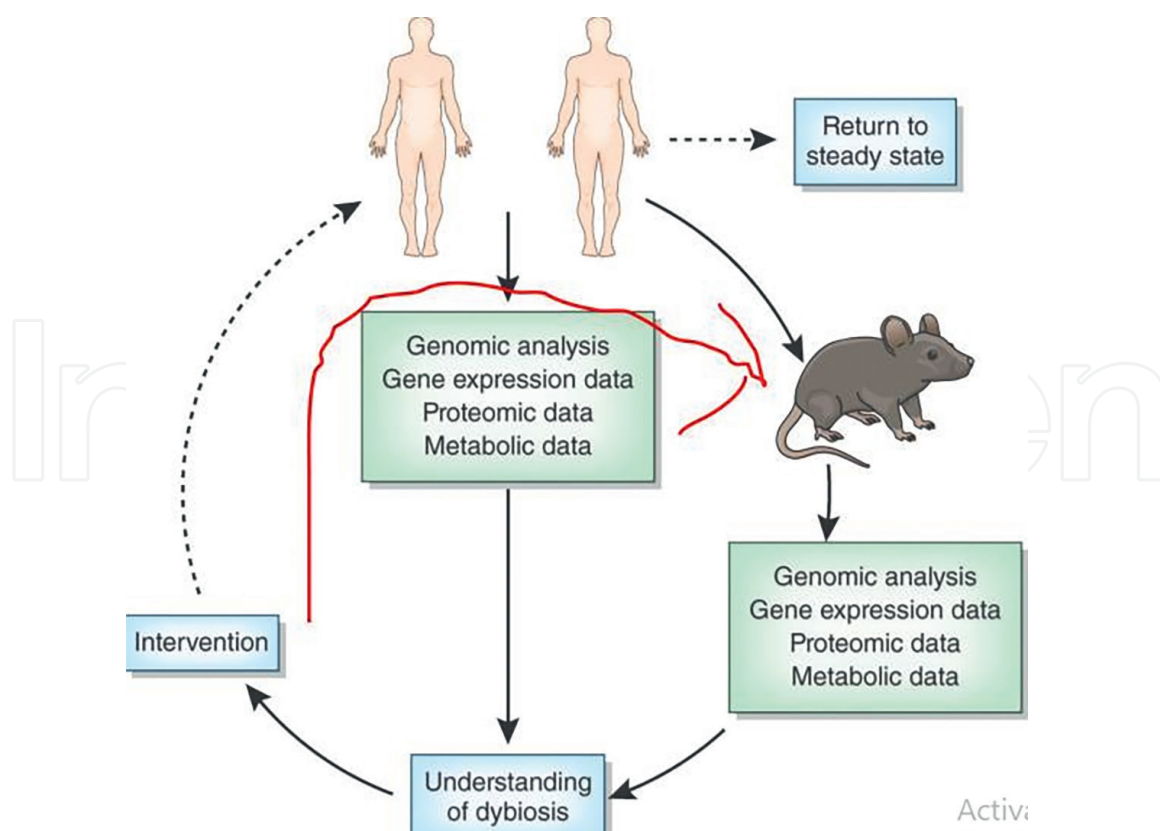


Figure 5. The iterative cycle of analysis, interpretation and translational intervention that facilitate moving microbiome research out of correlative observation and into therapeutic treatments [78].

10. Microbiome applications

Studying the human microbiome is helping researchers to understand how the body responds to different diets, diseases and drugs. The human microbiome can be seen of as a source of genetic variety, a disease modifier, a significant component of immunology, and a functional entity that regulates metabolism and modulates drug interactions. On the one hand, there are numerous possible probiotics or helpful bacteria that could help to prevent or treat various diseases, albeit most of them are now unavailable for cultivation [79]. Little was known about the variety of microorganisms that happily dwell inside and on our bodies more than a decade ago, but researchers today believe they have the potential to influence the future of human health and examining linkages between health and disease. Almost 70% of the bacteria that make up the human microbiota are uncultivable, and many of them are anaerobic (so can only be cultivated without oxygen). These barriers have prompted researchers to investigate meta-genomics and in vivo models. While in vitro models of the digestive tract can be used to simulate one or more stages of digestion (in the stomach, small intestine, or colon), they are still incapable of duplicating the complexity of host-microbiota interactions [80]. Therefore the recent scientific evidence suggests that a healthy and diverse microbiome is beneficial to human health and the microbiome is becoming a cornerstone of preventive medicine (**Figure 6**).

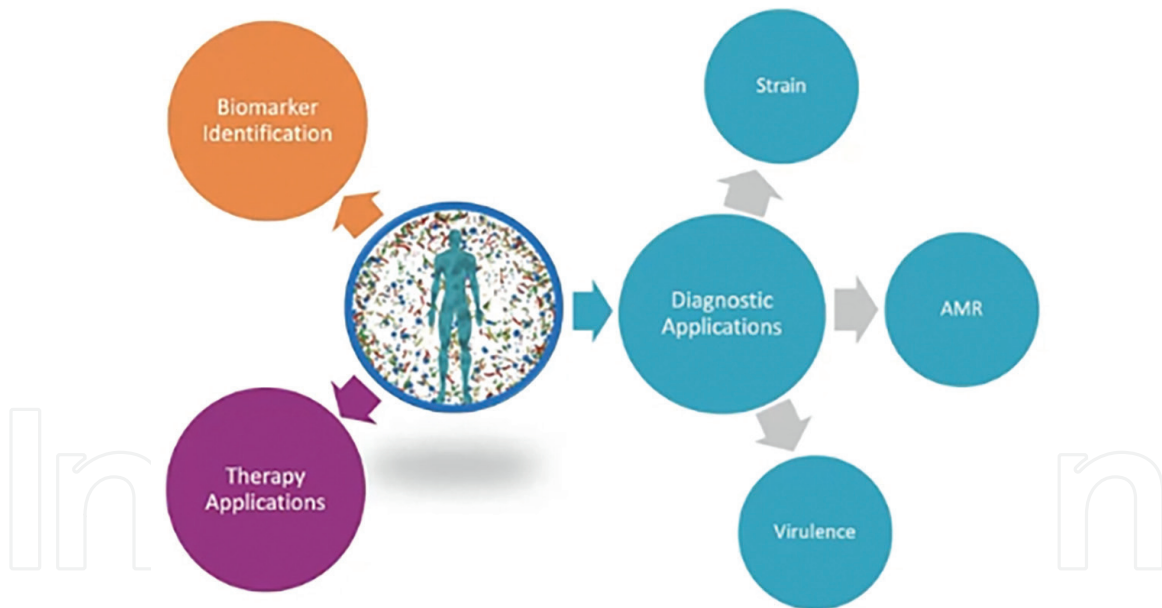


Figure 6.
The microbiome can be used to study, diagnose and treat diseases.

11. Conclusion

Microbiome research has made great progress in the past decades due to recent scientific advances in genetics and genomics. Consequently, despite being a relatively new field, microbiome has been successfully employed to alter microbiota and demonstrate promising prospects for therapeutics. It's worth noting that long-term usage of broad-spectrum antibiotics has the potential to damage the human microbiome. As a result, the indigenous microbial community becomes unbalanced,

allowing invading diseases to thrive. Treatments that include pre and probiotics, on the other hand, should be recommended. As a result, greater study into the use of probiotic therapy in the treatment of infectious diseases is needed. Indeed, our knowledge of the biology of complex diseases is expanding at an unprecedented rate and with unprecedented resolution, even as we recognize that what we have seen thus far is simply the tip of the iceberg, and that a large corpus of knowledge appears to be just around the corner. This should eventually lead to more effective treatments and prevention methods based on logical microbiota-based therapeutics. Therefore, researchers are using high throughput sequencing technologies and analytical methods, substantial advances have been achieved in both identifying the microbial taxa and understanding the relationship between microbiome composition and host phenotype, providing mechanistic insight on which microbes may be beneficial or which may be detrimental to one's health and given each microbiome is unique to an individual, this represents how high throughput sequencing technologies is impacting the future of personalized medicine and animal health, enhanced crop yield and nutritional quality, and the control of various pests and disease agents. In similar way, a complex microbiome minimizes the risk of some diseases, and probiotics can help with symptoms like IBS and eczema. Current tools and understanding of the microbiome have enabled researchers to develop new strategies to leverage applications of the microbiome. Overall, the grand vision of applied microbiome research is to improve health of humans, animals, plants, and whole ecosystem.

12. Future prospectus of microbiome

Microbiome research generates a large quantity of data, which necessitates the use of advanced computational techniques, which are rapidly evolving. Furthermore, many of the existing mathematical tools analyze connection rather than causation. As a result, researchers should remember that microbiome characterization, data analysis, and modelling are only a small part of the discovery process, and that they should be used in conjunction with traditional *in vitro* and *in vivo* model studies to prove cause and effect. To advance microbiome research into the therapeutic domain, researchers must go beyond clinical association studies to validate their models in other clinical cohorts and understand the mechanisms of causation *in vitro*, *ex vivo*, and animal model systems. While metagenomic studies have revealed immense diversity, additional tools are required to understand the community structure, function, and their interaction with host environments. Using microbiome analysis with Next generation sequencing to help define biomarkers and stratify patient populations, which may help improve therapeutic outcomes in the future. In addition, gaining deeper understanding of the microbiome through improved tools and methods will enable engineers and innovators to develop better applications and unlock the potential of the microbiome. As a result, pre/probiotics are likely to be coupled with other dietary substances to generate a more powerful health benefit. Furthermore, merging multiple study disciplines and employing new technological approaches in microbiome research is predicted to open the way for the development of evidence-based clinical therapies for modern-day health challenges. Previous research has found that bacteria have 35.5 million functions, of which just 0.02% are known, according to computational predictions. Despite the growing body of research on the microbiome, our understanding of its function, particularly how it influences health and disease, is limited because to the lack of a “universal” standard for study comparability.

The microbiome has been the subject of significant attempts to unravel all of its genetic information for the benefit of humankind, which requires worldwide coordination. Ultimately, new clinical tools and applications should be developed, as each individual and every population requires more individualized and effective care.

Conflict of interest


The authors declare that they have no conflict of interest.

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